PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT
(PCT Rule 71.1)

Date of mailing *(day/month/year)*	30.03.2004
Applicant's or agent's file reference AS/PG4715 WO	**IMPORTANT NOTIFICATION**

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/GB 03/01595	10.04.2003	13.04.2002

Applicant
GLAXO GROUP LIMITED et al

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(5), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Hutterer, G Tel. +49 89 2399-8066

Form PCT/IPEA/416 (January 2004)

Express Mail Label No.
EV332062937US

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference AS/PG4715 WO	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/GB 03/01595	International filing date *(day/month/year)* 10.04.2003	Priority date *(day/month/year)* 13.04.2002
International Patent Classification (IPC) or both national classification and IPC A61K9/00		
Applicant GLAXO GROUP LIMITED et al		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 1 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
24.10.2003	30.03.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Hedegaard, A Telephone No. +49 89 2399-8644

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB 03/01595

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-14	as originally filed

Claims, Numbers

1-15, 16 (part), 25-30	as originally filed
16 (part), 17-24	received on 29.01.2004 with letter of 29.01.2004

Drawings, Sheets

1/2-2/2	as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   - ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
   - ☐ the language of publication of the international application (under Rule 48.3(b)).
   - ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   - ☐ contained in the international application in written form.
   - ☐ filed together with the international application in computer readable form.
   - ☐ furnished subsequently to this Authority in written form.
   - ☐ furnished subsequently to this Authority in computer readable form.
   - ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
   - ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   - ☐ the description, pages:
   - ☐ the claims, Nos.:
   - ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 12

   because:

   ☒ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   see separate sheet

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-24
	No:	Claims	
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-24
Industrial applicability (IA)	Yes:	Claims	1-11,13-24
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Section III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. Claim 12 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability, novelty and inventive step of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

Re Section V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following documents:

   D1: EP-A-0 416 951
   D2: WO 02 15876 A

2. The subject-matter of claims 1-11 (composition), 12 (method), 13 (use), 14-15 (device), 16-21 (pack), 22-24 (use) is novel (Art. 33(2) PCT) since a dry powder composition comprising salmeterol, fluticasone propionate and a derivatised carbohydrate has not been disclosed in the available prior art documents.

3. The problem of the present application was to improve bioavailability of dry powder compositions for inhalation comprising salmeterol and fluticasone propionate.

   This problem is solved by incorporating a derivatised carbohydrate in particulate form (see claim 1).

   D1 (see examples 6-11) discloses dry powder formulations comprising salmeterol, fluticasone propionate and lactose. The subject-matter of present claim 1 differs

therefrom in that the carbohydrate is derivatised.

However, it is known from D2 (see p. 1, l. 3-4 and p. 5, l. 23-24) that amorphous hydrophobically derivatised carbohydrate (HDC) demonstrates an improved emitted dose uniformity compared to both crystalline trehalose and lactose in dry powder formulations for inhalation. D2 refers to HDC as a carrier and not as a stabiliser. However, this does not change the fact that the obtained effect is the same in D2 as well as in the present application, namely improved dose uniformity.

It therefore appears to be obvious for the skilled person, faced with the above-mentioned problem, to incorporate a derivatised carbohydrate in particulate form in the compositions according to D1 and, thus, to arrive at the compositions according to present claim 1. Hence, in the absence of any unexpected effects, the subject-matter of claim 1 is not considered to involve an inventive step (Art. 33(3) PCT).

4. The same applies mutatis mutandis to independent claims 12, 13, 14, 16, 22 and 23.

5. A positive international preliminary report for the subject-matter of the dependent claims can only be established when they refer to independent claims which meet the requirements of the PCT.

6. For the assessment of the present claim 12 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

a plurality of containers, each container having therein an inhalable composition according to any one of claims 1 – 10.

17. A medicament pack according to claim 16 wherein the strip is sufficiently flexible to be wound into a roll.

18. A medicament pack according to claim 16 wherein the lid sheet and base sheet have leading end portions which are not sealed to one another.

19. A medicament pack according to claim 18 wherein at least one of the said leading end portions is constructed to be attached to a winding means.

20. A medicament pack according to claim 16 wherein the hermetic seal between the base and lid sheets extends over their whole width.

21. A medicament pack according to claim 16 wherein the lid sheet may be peeled from the base sheet in a longitudinal direction from a first end of the said base sheet.

22. The use of particulate derivatised carbohydrates in dry powder pharmaceutical compositions comprising salmeterol or a pharmaceutically acceptable salt thereof and fluticasone propionate in order to improve stability performance.

23. The use of particulate derivatised carbohydrates in dry powder pharmaceutical compositions comprising salmeterol or a pharmaceutically acceptable salt thereof and fluticasone propionate in order to eliminate or reduce the detrimental effect on fine particle dose caused on storage of said compositions.

24. The use according to claim 22 or 23 in which the particulate derivatised carbohydrate is cellobiose octaacetate.